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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/486,757	07/03/2000	TONI M. KUTCHAN	J&J-1673	4581

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ONE JOHNSON & JOHNSON PLAZA  
NEW BRUNSWICK, NJ 08933-7003

EXAMINER

ZARA, JANE J

ART UNIT	PAPER NUMBER
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1635

DATE MAILED: 01/02/2002

15

Please find below and/or attached an Office communication concerning this application or proceeding.

**Office Action Summary**

Application No.

09/486,757

Applicant(s)

KUTCHAN

Examiner

Jane Zara

Art Unit

1635

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

**Period for Reply**

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133)
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

**Status**

- 1) ☐ Responsive to communication(s) filed on \_\_\_\_.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

**Disposition of Claims**

- 4) ☒ Claim(s) 1-62 is/are pending in the application.
- 4a) Of the above claim(s) 1-56 is/are withdrawn from consideration.
- 5) ☐ Claim(s) \_\_\_\_ is/are allowed.
- 6) ☒ Claim(s) 56-62 is/are rejected.
- 7) ☐ Claim(s) \_\_\_\_ is/are objected to.
- 8) ☐ Claim(s) \_\_\_\_ are subject to restriction and/or election requirement.

**Application Papers**

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on \_\_\_\_ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
- Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
- 11) ☐ The proposed drawing correction filed on \_\_\_\_ is: a) ☐ approved b) ☐ disapproved by the Examiner.
- If approved, corrected drawings are required in reply to this Office action.
- 12) ☐ The oath or declaration is objected to by the Examiner.

**Priority under 35 U.S.C. §§ 119 and 120**

- 13) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some \* c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. \_\_\_\_.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
- \* See the attached detailed Office action for a list of the certified copies not received.
- 14) ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).
- a) ☐ The translation of the foreign language provisional application has been received.
- 15) ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

**Attachment(s)**

- 1) ☐ Notice of References Cited (PTO-892)
- 2) ☒ Notice of Draftsperson's Patent Drawing Review (PTO-948)
- 3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) 7.
- 4) ☐ Interview Summary (PTO-413) Paper No(s). \_\_\_\_.
- 5) ☐ Notice of Informal Patent Application (PTO-152)
- 6) ☒ Other: *See Continuation Sheet*.

Continuation of Attachment(s) 6). Other: Notice to Comply & Raw Seq. Listing.

File

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### DETAILED ACTION

Claims 1-62 are pending in the instant application.

#### *Election/Restriction*

Claims 1-56 are withdrawn from further consideration pursuant to 37 CFR 1.142(b) as being drawn to a nonelected invention, there being no allowable generic or linking claim.

Election was made **without** traverse in Paper Nos. 9 and 12.

Applicant's election without traverse of Group V, and SEQ ID NO: 10 in Paper Nos. 9 and 12 is acknowledged.

#### *Sequence Compliance*

This application contains sequence disclosures that are encompassed by the definitions for nucleotide and/or amino acid sequences set forth in 37 CFR 1.821(a)(1) and (a)(2). However, this application fails to comply with the requirements of 37 CFR 1.821 through 1.825 for the reason(s) set forth on the attached Notice To Comply With Requirements For Patent Applications Containing Nucleotide Sequence And/Or Amino Acid Sequence Disclosures.

**Please see page 5 of the attached raw sequence listing to ensure that the submitted sequences comply in fields < 220> and <223>. Please identify at appropriate places in the specification which SEQ ID Nos. have been used to obtain successful expression of recombinant P-450 reductase.** See the accompanying Notice to Comply. Direct the reply to the undersigned. Applicant is requested to return a copy of the attached Notice to Comply with the reply.

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***Claim Rejections - 35 USC § 112***

The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 57-62 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

The claims are drawn to alkaloids and methods of producing them, which alkaloids have been obtained from a stand of stably reproducing alkaloid poppies transformed with the polynucleotide of SEQ ID NO: 10 or variants thereof, which polynucleotide encodes a cytochrome P-450 reductase.

The following factors have been considered in determining that the specification does not enable the skilled artisan to make and/or use the invention claimed. This determination is based on several factors which, when considered together, illustrate that the art of enhancing alkaloid production in straw comprising enhancing the expression of cytochrome P-450 reductase is in its infancy and highly unpredictable.

**The nature of the invention.** The claimed invention is drawn to methods of enhancing the expression and yield of alkaloids from straw of poppy plants by increasing the expression of a cytochrome P-450 reductase enzyme following its stable transfection into the plants.

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**The state of the prior art and the predictability or unpredictability of the art.**

Increased alkaloid yields in poppy straw require systematically (or serendipitously) identifying the limiting step(s) that must be overcome in obtaining enhanced alkaloid expression. It is hypothesized currently that one limiting factor in the ability to increase alkaloid production in poppy plants is due to a limited amount of appropriate P-450 reductase. However, P-450 reductase is not the only enzyme involved in alkaloid metabolism, and overexpressing the claimed P-450 reductase does not necessarily ensure that the bottlenecks that have been historically encountered in attempts to increase alkaloid yields from poppy straw will be overcome. This may require the overexpression and orchestration of various enzymes involved in alkaloid biosynthesis, and must be determined empirically.

**The amount of direction or guidance presented in the specification AND the presence or absence of working examples.** Applicants have not provided guidance in the specification toward a method of obtaining enhanced yields of alkaloids from poppy straw comprising the stable expression of transfected nucleic acids encoded by SEQ ID NO: 10, or any variants thereof. The specification teaches the transformation of poppy plant cells with recombinant cytochrome P-450 reductase of undisclosed SEQ ID Nos. (i.e. no SEQ ID Nos. have been listed in the results of the instant specification). The specification also teaches the subsequent growth of plantlets obtained from the embryos which resulted from transformed plant cells in culture medium. The specification fails to teach the successful generation and harvesting of increased yields of alkaloids from the straw of transduced poppy plants. One

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skilled in the art would not accept on its face the examples given in the specification of the transformation of plant cells with recombinant P-450 reductase and subsequent plantlet generation as being correlative or representative of the successful generation and harvesting of increased yields of alkaloids from poppy straw, which straw had been transduced with recombinant P-450 reductase in view of the lack of guidance in the specification and known unpredictability associated with overcoming the bottlenecks historically encountered in attempts to increase the production of alkaloids in poppy plants. The specification as filed fails to provide any particular guidance which resolves the known unpredictability in the art associated with overexpressing one recombinant enzyme which may be involved (among several enzymes) in the biosynthesis of a product and increasing yields of the product.

**The breadth of the claims and the quantity of experimentation required.** The breadth of the claims is very broad. The claims are drawn to alkaloids and methods of producing them, which alkaloids have been obtained from a stand of stably reproducing alkaloid poppies transformed with the polynucleotide of SEQ ID NO: 10 or variants thereof, which polynucleotide encodes a cytochrome P-450 reductase. In order to practice the invention claimed, it would require undue trial and error and undue experimentation beyond which is taught in the specification to practice the invention drawn to increasing the yield of alkaloids in poppy straw by stably overexpressing the P-450 reductase encoded by SEQ ID NO: 10, as well as by a representative number of sequence variants of SEQ ID NO: 10 in poppy plants. The quantity of experimentation required to practice the invention as claimed would require the *de novo*

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determination of comparisons in alkaloid yields between transformed and untransformed poppy straw. Since the specification fails to provide any particular guidance for the successful increased yield of alkaloids in poppy straw obtained from poppy plants comprising stably transformed and appropriately expressed P-450 reductase encoded by SEQ ID NO: 10, or any representative number of variants thereof, and since determination of these factors is highly unpredictable, it would require undue experimentation to practice the invention claimed.



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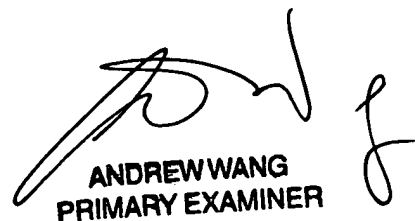
*Conclusion*

Certain papers related to this application may be submitted to Art Unit 1635 by facsimile transmission. The faxing of such papers must conform with the notices published in the Official Gazette, 1156 OG 61 (November 16, 1993) and 1157 OG 94 (December 28, 1993) (see 37 C.F.R. § 1.6(d)). The official fax telephone numbers for the Group are (703) 308-4242 and (703) 305-3014. NOTE: If Applicant *does* submit a paper by fax, the original signed copy should be retained by applicant or applicant's representative. NO DUPLICATE COPIES SHOULD BE SUBMITTED so as to avoid the processing of duplicate papers in the Office.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to **Jane Zara** whose telephone number is (703) 306-5820. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, John LeGuyader, can be reached on (703) 308-0447. Any inquiry regarding this application should be directed to the patent analyst, Katrina Turner, whose telephone number is (703) 305-3413. Any inquiry of a general nature or relating to the status of this application should be directed to the Group receptionist whose telephone number is (703) 308-0196.

*JZ*

December 28, 2001

  
ANDREW WANG  
PRIMARY EXAMINER